Center Reflections

A monthly publication highlighting activities at the W.M. Keck Foundation Center for Molecular Structure

California State University Fullerton

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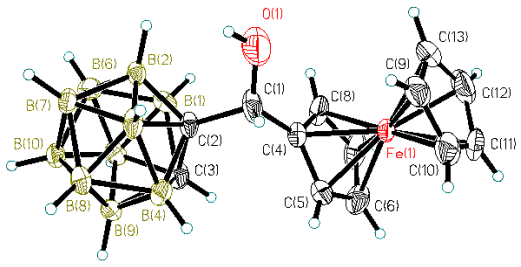
Structure Determinations and Molecular Modeling of Novel and Hard to Obtain Carborane Compounds

CSU Los Angeles

The addition of o-carborane to electrophiles is one of the most important reactions to synthesize carboranes containing organic functional groups which could be useful as multifunctional molecules for material science and/or as boron carriers for boron neutron capture therapy (BNCT). Lithiocarboranes which are readily prepared from lithium-containing reagents and carboranes are widely utilized for C-C bond formation of various functional groups with carboranes. In the synthesis of many monosubstituted carboranes a multi-step synthesis is required involving the t-butyldimethylsilyl-carborane synthon. Although this precursor has been utilized in the formation of a number of monosubstituted species facile routes to derivatized carboranes is still a problem. Prof. Frank Gomez and his group at CSU Los Angeles have focused on developing the use of tetrabutylammonium fluoride (TBAF) in the reaction of o-carborane derivatives with aldehydes. They have shown that facile reaction of o-carborane with aldehydes and TBAF in THF gives high yields of secondary alcohol carborane derivatives. The novel 1-methylhydroxy-(cyclopentadienyl (cyclopentadienyl)iron)-1,2-dicarba-closo dodecaborane[1], was synthesized in 55% yield from ferrocenecarboxaldehyde and o-carborane with TBAF. Work continues in extending the versatility of this technique by examining the reaction of disubstituted aldehydes and o-carborane.



The W.M. Keck Foundation Center for Molecular Structure (CMolS) has provided the facilities and expertise for solving the structure. This very unique species proves the formation of difficult to obtain sterically encumbered monosubstituted carboranes. CMolS has given students experience in the use of state-of-the-art crystallographic facilities and techniques. Chuautemoc Arellanes (NIH-MBRS), who conducted this re-

search as an undergraduate with Gomez at CSULA, is currently in the Ph.D. program at UCLA. The interaction with CMolS was one reason he chose to go to graduate school.

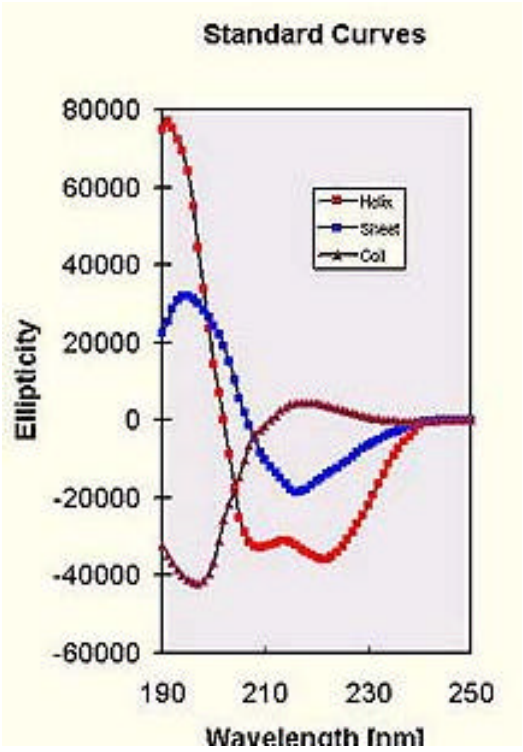
Dr. Frank A. Gomez is Associate Professor of Chemistry at California State University, Los Angeles (CSULA). He received his B.S. in chemistry in 1986 from CSULA and his Ph.D. in chemistry from the University of California, Los Angeles (UCLA) in 1991, where he was a National Institutes of Health Predoctoral Fellow. From 1991-1994 he was a Damon Runyon-Walter Winchell Cancer Research Fund Postdoctoral Fellow in the Department of Chemistry at Harvard University. Dr. Gomez' research interests include the use of capillary electrophoresis (CE) in the analysis of biological problems with a particular interest in molecular recognition and analysis of in-capillary enzyme-mediated transformations as well as main-group synthetic chemistry.

1. Chuahtemoc Arellanes, Frank Gomez, Guy Crundwell and Katherine Kantardjieff "The crystal structure of 1-methylhydroxy-(cyclopentadienyl (cyclopentadienyl)iron)-1,2-dicarba-*closo*-dodecacarborane at 213K. " Acta Cryst. C54 (1998).

Remote Access to Instrumentation: Circular Dichroism Spectropolarimetry

CSU Long Beach

Prof. Jeffrey Cohlberg and his students at CSU Long Beach are studying the specificity of coiled coil dimer formation among neurofilament proteins and the roles of the various domains of the proteins in dimer stability. Both homodimers and heterodimers formed from neurofilament proteins or pairs of neurofilament proteins are being examined in CD melting experiments. We work with intact neurofilament proteins, with the isolated rod domains which form the coiled coil structure, and with various other truncated and chimeric constructs. The melting points of the various complexes provide information about the thermodynamic stability of the various coiled coil dimers.



http://www-structure.llnl.gov/cd/cdtutorial/htm

The experiments are done on the CD at CSUF, equipped with a computer controlled Neslab temperature bath which was funded by a grant from the National Science Foundation. Cohlberg's lab computer at CSULB communicates with the computer attached to the CD at CSUF by pcANYWHERE™. This enables members of his group to come to CSUF, load a sample and start a preprogrammed melting experiment, then return to CSULB, where they can monitor the course of the experiment and retrieve and process the data after the experiment is over. Anne Simonson, a student in the MS in Biochemistry program, is currently working on this project.

Jeffrey Cohlberg, a native of Philadelphia, received a B. A. with Distinction in Chemistry from Cornell University in 1966 and was awarded membership in Phi Beta Kappa. His doctoral thesis, describing studies on the structure and assembly of the allosteric enzyme aspartate transcarbamylase, earned him a Ph. D. in Biochemistry from the University of California at Berkeley in 1972. As an NIH Postdoctoral Fellow at the Institute for Enzyme Research of the University of Wisconsin, from 1972 to 1975, he studied the structure and assembly of bacterial ribosomes. In 1975 he joined the faculty of the Department of Chemistry and Biochemistry at California State University, Long Beach. His work on intermediates in cytokeratin assembly, as a Visiting Research Professor at the German Cancer Research Center in Heidelberg from 1982 to 1983, was the beginning of his involvement in research on the intermediate filaments of the mammalian cytoskeleton. A second sabbatical leave was spent at the College de France in Paris from 1992 to 1993. Dr. Cohlberg's research on the structure and assembly of neurofilaments has been supported by the National Science Foundation since 1985. In 1997 he was named a Dreyfus Scholar by the Henry and Camille Dreyfus Foundation. In 1998 he was named Most Valuable Professor by the outstanding graduating senior of the College of Natural Sciences and Mathematics at Cal State Long Beach.

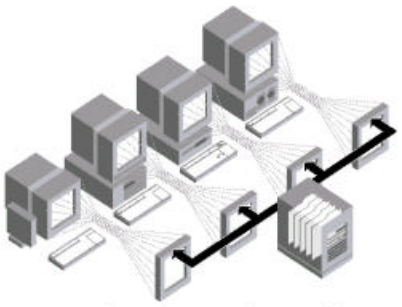
Remote Access to Instrumentation: X-ray Crystallography

The rapid development of the information superhighway and the world wide web has revolutionized the telecommunications system and presents a great opportunity to universities such as the California State University (CSU) to restructure and globalize formal education by offering novel web-based courses, tutorials and virtual laboratories that require specialized instrumentation and expertise. Through the power of the Internet via remote access and distance teaching/learning, we are extending distance learning and remote access to include instructional and research laboratory experiences in x-ray crystallography. In this 'Virtual Laboratory' students can conduct experiments at their home campuses, at their own pace, with pre-acquired datasets. Students will be able to access Internet-based laboratory materials in the form of online lab manuals, courseware, interactive tutorials, and reporting templates. Students will also have the capability to conduct independent research projects through our remote access data acquisition system.

A recent NIH Structural Biology report (July 1998) indicates that high throughput crystallography is a high priority. Mandated by this report are the development of data collection and analysis using modern distributed computing, and robotics for automated screening and monitoring of samples. Recognizing that distance learning and remote access is an exciting new area of education, CMolS has taken a leadership role in the CSU in developing an advanced and computer-driven system to serve the needs of distance education and research in x-ray crystallography. CMolS began providing undergraduate researchers remote access to x-ray diffraction instrumentation in 1998 by adopting a simple remote access technology using pcANYWHERE™ running under WindowsNT™. Students and faculty have shared access to data files and can have remote access to the diffractometers. Several campuses have contributed funds for purchase of the Cambridge Structure Database, the NIST Database and site licenses for SHELXTL™ for solving structures.

Crystallography has always pushed technology to the limits of what it can accomplish. Computer graphics was pioneered 25 years ago in an attempt to model structures efficiently. Today's large-format detectors scan in seconds, allowing rapid characterization of a large number of structures. We are proposing to the National Science Foundation a new computing environment to support high throughput experiments at CMolS, which is modeled after an NIH collaboratory program being developed at the Stanford Synchrotron Radiation Laboratory (SSRL). Our proposed sever-based computing environment will allow more students and faculty to take full advantage of the technology at CMolS for both education and research using remote access. A team of student and faculty researchers distributed anywhere in the CSU will have access to the tools at CMolS to perform a complete crystallography experiment, from data collection to final structure.

Their experiment will begin at the x-ray source. Using the CITRIX ICA™ Client and Metaframe™ Server, they will use a mechanical robotic arm to mount, center and change samples. The individual sample will be visible to the remote research student via the image grabber software. Students can then take control of diffractometers at CMolS, design a data collection strategy, set up data collection and monitor progress of data acquisition. Users will be able to videoconference with their home campuses over a high speed network, or they can control their experiment from a remote location. Then, users will be given the option of either a) transferring their data to their remote location for remote processing or b) performing all the calculations on the CMolS server, accessible over the Internet. A familiar set of programs for data collection strategy planning, sample manipulation, data collection control, data processing and refinement, and structure solution will be available to students and faculty. These programs will be organized in a manner that facilitates documentation of project work, permanent archiving and easy and retrieval of data. Sample files and interactive tutorials will also be available for instructional purposes.



In server-based computing, multi-user capabilities allow applications and data to be deployed, managed, supported and executed 100% on the server.

Distance learning and remote access networks make highly specialized training available without the geographical and financial limitations of local training. Distance learning and remote access networks provide an innovative and effective teaching and learning environment. Students with remote access have the best materials on computer and the best instructors available to deliver lectures and assist with research experiments requiring specialized instrumentation and expertise. Exploring the possibilities afforded by remote learning curricula can lead to inspiring and collaborative projects in molecular structure.

Through its networks and partnerships, CMolS is enhancing the research and education infrastructure in the CSU and making a significant contribution to the professional development of faculty and a new generation of scientists. One further benefit that students have reaped from this project is the collaborative nature of science, an aspect of research of which students are rarely aware.

Upcoming Events

April 27, 1999: "Molecular Crystallography Then and Now". Seminar given by Prof. Katherine Kantardjieff at **CSU Fresno**.

April 29, 1999: "A History of Women in Science". Lecture given by Prof. Katherine Kantardjieff at the monthly dinner meeting of the San Gorgonio Section of the **American Chemical Society**.

May 22-26, 1999: **American Crystallographic Association** National Meeting, Buffalo, NY. http://nexus.hwi.buffalo.edu/ACA/ACA-Annual/Buffalo/Buffalo.html

June 26-28, 1999: **Computational Science Workshop**, San Diego State University. http://www.edcenter.sdsu.edu/training/workshop/events.html

July 8-10, 1999: **CSU Computational Chemistry Council** Summer Conference, Humboldt State University. http://www.humboldt.edu/~chemcomp/

August 4-13, 1999: **International Union of Crystallography** Meeting, Glasgow, Scotland. http://www.iucr.org/

August 22 - 26, 1999: **American Chemical Society** National Meeting, New Orleans, LA. http://www.acs.org/meetings/neworleans/welcome.htm

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